

09/288,556

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 18:17:26 ON 10 JUL 2003

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 18:17:41 ON 10 JUL 2003

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STRUCTURE FILE UPDATES: 9 JUL 2003 HIGHEST RN 545225-95-4

DICTIONARY FILE UPDATES: 9 JUL 2003 HIGHEST RN 545225-95-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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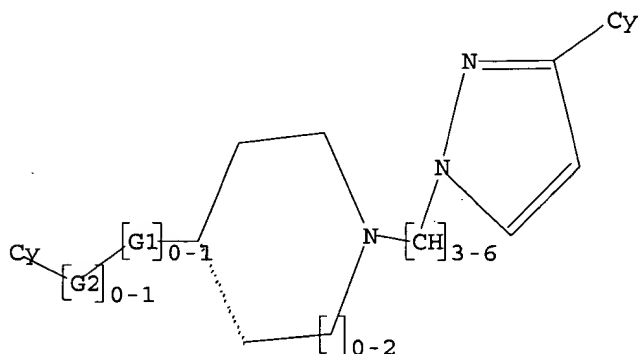
Uploading 927324.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 C,O,S,N

G2 C,N

09/288,556

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 18:18:14 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 969 TO ITERATE

100.0% PROCESSED 969 ITERATIONS 16 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 17513 TO 21247  
PROJECTED ANSWERS: 80 TO 560

L2 16 SEA SSS SAM L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.60	1.81

FILE 'CAPLUS' ENTERED AT 18:20:20 ON 10 JUL 2003  
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FILE COVERS 1907 - 10 Jul 2003 VOL 139 ISS 2  
FILE LAST UPDATED: 9 Jul 2003 (20030709/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2

L3 4 L2

=> d l3 1-4 ibib abs hitstr

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS

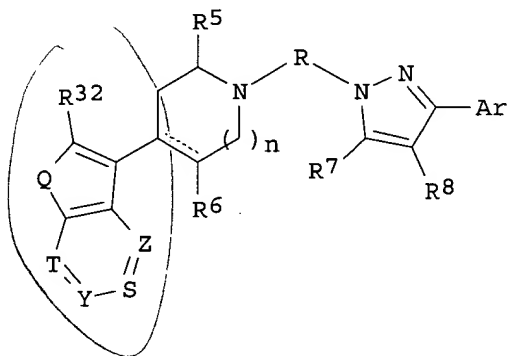
ACCESSION NUMBER: 2002:184900 CAPLUS  
DOCUMENT NUMBER: 136:247577  
TITLE: Preparation of 3-phenyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as cathepsin S inhibitors for treating allergies  
INVENTOR(S): Cai, Hui; Edwards, James P.; Gu, Yin; Karlsson, Lars; Meduna, Steven P.; Pio, Barbara A.; Sun, Siqun; Thurmond, Robin L.; Wei, Jianmei  
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA  
SOURCE: PCT Int. Appl., 115 pp.  
CODEN: PIXXD2

09/288,556

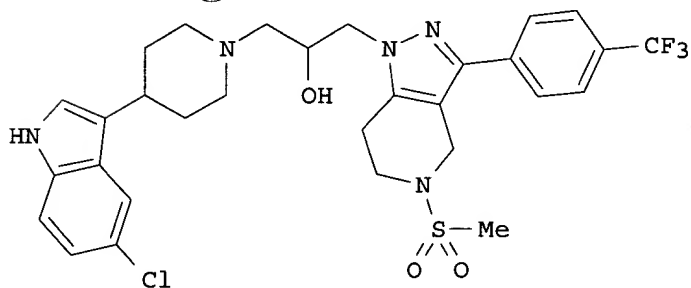
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 8  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020013	A2	20020314	WO 2001-US27480	20010905
WO 2002020013	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002040019	A1	20020404	US 2001-927188	20010810
AU 2001088731	A5	20020322	AU 2001-88731	20010905
EP 1315492	A2	20030604	EP 2001-968487	20010905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2000-230407P	P 20000906
			US 2001-927188	A 20010810
			US 2000-225178P	P 20000814
			WO 2001-US27480	W 20010905

OTHER SOURCE(S): MARPAT 136:247577  
GI



I



II

AB Title compds. I [wherein Ar = (un)substituted mono- or bicyclic (hetero)aryl; G = (un)substituted alkenediyl or alkanediyl; Q = O, S, or (un)substituted N; S, T, Y, and Z = independently N or (un)substituted C;

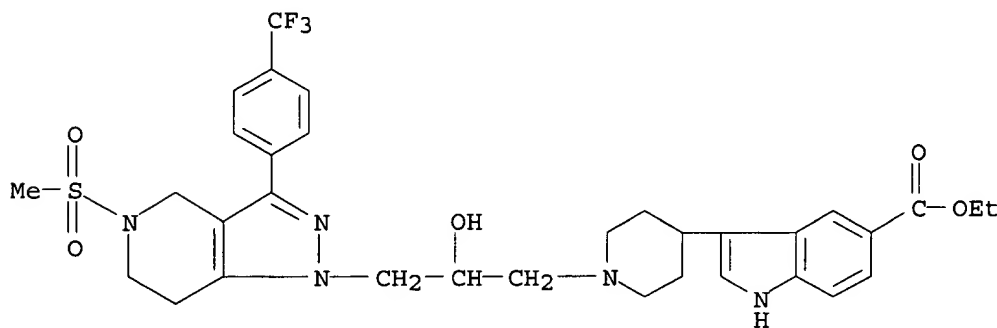
R5 and R6 = independently H or alkyl; R7 and R8 = independently H, alkyl, alkenyl, alkoxy, alkylthio, halo, carbocyclyl, or heterocyclyl; or R7R8 = (un)substituted carbocyclic or heterocyclic ring; R32 = H, (hydroxy)alkyl, CN, acyl, carbamoyl, CHO, or alkoxycarbonyl; n = 0-2; or pharmaceutically acceptable salts, amides, esters, or stereoisomers thereof] were prepd. as cathepsin S inhibitors for the treatment of an allergic condition, including an atopic allergic conditions. For example, 1-methanesulfonylpiperidin-4-one (prepn. given) was condensed with morpholine in the presence of TSOH to give the enamine. Reaction with 4-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>COCl, followed by cycloaddn. with H<sub>2</sub>NNH<sub>2</sub>, gave 5-methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine (72%). Alkylation with epichlorohydrin (35%) and addn. of 5-chloro-3-piperidin-4-yl-1H-indole (prepn. given) afforded II (88%). The latter inhibited recombinant human cathepsin S with IC<sub>50</sub> of 0.07 .mu.M.

IT 400801-53-8P, 3-(1-[2-Hydroxy-3-[5-methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl]-piperidin-4-yl)-1H-indole-5-carboxylic acid ethyl ester  
400801-58-3P, 1-[5-Methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-3-[4-(5-oxy-1H-pyrrolo[3,2-c]pyridin-3-yl)-piperidin-1-yl]-propan-2-ol  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antiallergy agent; prepn. of phenylpyrazolopyridine antiallergy agents from piperidinones, benzoyl chlorides, and hydrazine)

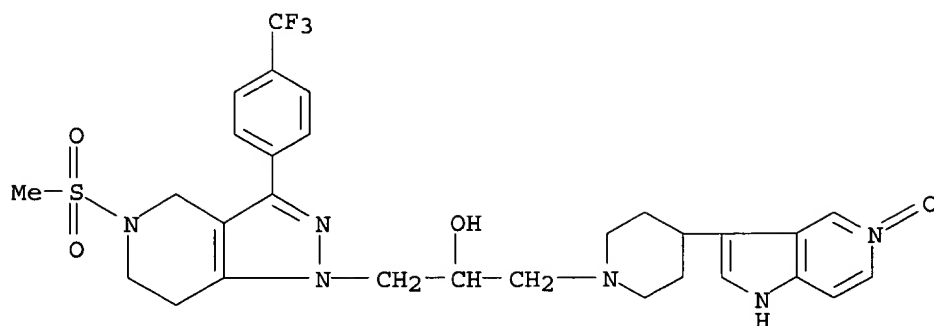
RN 400801-53-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[1-[2-hydroxy-3-[4,5,6,7-tetrahydro-5-(methylsulfonyl)-3-[4-(trifluoromethyl)phenyl]-1H-pyrazolo[4,3-c]pyridin-1-yl]propyl]-4-piperidinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 400801-58-3 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 4,5,6,7-tetrahydro-5-(methylsulfonyl)-.alpha.-[[4-(5-oxido-1H-pyrrolo[3,2-c]pyridin-3-yl)-1-piperidinyl]methyl]-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:184898 CAPLUS

DOCUMENT NUMBER: 136:247575

TITLE: Preparation of 3-phenyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as cathepsin S inhibitors for treating allergies

INVENTOR(S): Butler, Christopher R.; Cai, Hui; Edwards, James P.; Grice, Cheryl A.; Gu, Yin; Gustin, Darin J.; Karlsson, Lars; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sehon, Clark A.; Sun, Siquan; Tays, Kevin L.; Thurmond, Robin L.; Wei, Jianmei

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 165 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

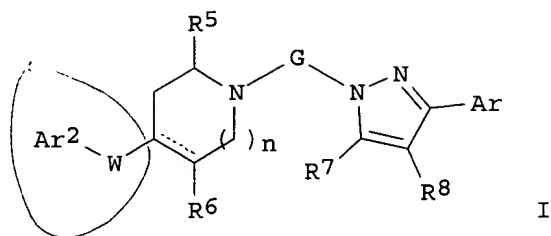
applicants

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020011	A2	20020314	WO 2001-US27429	20010905
WO 2002020011	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003078419	A1	20030424	US 2001-927324	20010810
AU 2001088706	A5	20020322	AU 2001-88706	20010905
EP 1315490	A2	20030604	EP 2001-968461	20010905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

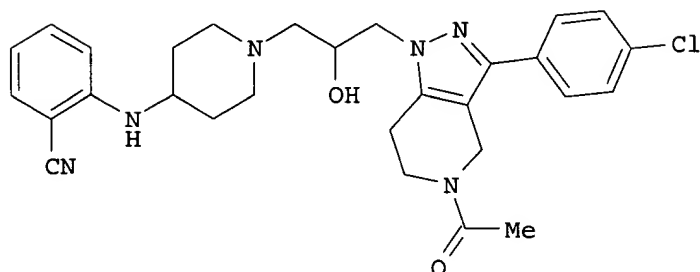
PRIORITY APPLN. INFO.: US 2000-230407P P 20000906  
US 2001-927324 A 20010810  
US 2000-225178P P 20000814  
WO 2001-US27429 W 20010905

OTHER SOURCE(S): MARPAT 136:247575

GI



I



II

AB Title compds. I [wherein Ar and Ar<sub>2</sub> = independently (un)substituted mono- or bicyclic (hetero)aryl; G = (un)substituted alkenediyl or alkanediyl; W = O, S, (un)substituted N or CH, CO, CONH, NHCO, or a bond; R<sub>5</sub> and R<sub>6</sub> = independently H or alkyl; R<sub>7</sub> and R<sub>8</sub> = independently H, alkyl, alkenyl, alkoxy, alkylthio, halo, or (un)substituted carbocyclyl or heterocyclyl; or R<sub>7</sub>R<sub>8</sub> form an (un)substituted carbocyclic or heterocyclic ring; R<sub>z</sub> = H, OH, or is absent; n = 0-2; or pharmaceutically acceptable salts, amides, esters, or stereoisomers thereof] were prep'd. as cathepsin S inhibitors for the treatment of an allergic condition, including an atopic allergic conditions. For example, N-acetyl-4-piperidone was condensed with morpholine in the presence of TSOH to give the enamine. Reaction with 4-ClC<sub>6</sub>H<sub>4</sub>COCl and cycloaddn. of the product with H<sub>2</sub>NNH<sub>2</sub> gave 1-[3-(4-chlorophenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone (42%). Alkylation with epichlorohydrin (60%), followed by addn. of 1,4-dioxo-8-azaspiro[4.5]decane (81%), conversion to the piperidinone (65%), and reductive addn. of 2-aminobenzonitrile (20%), afforded II. The latter inhibited recombinant human cathepsin S with IC<sub>50</sub> of 0.73 .mu.M.

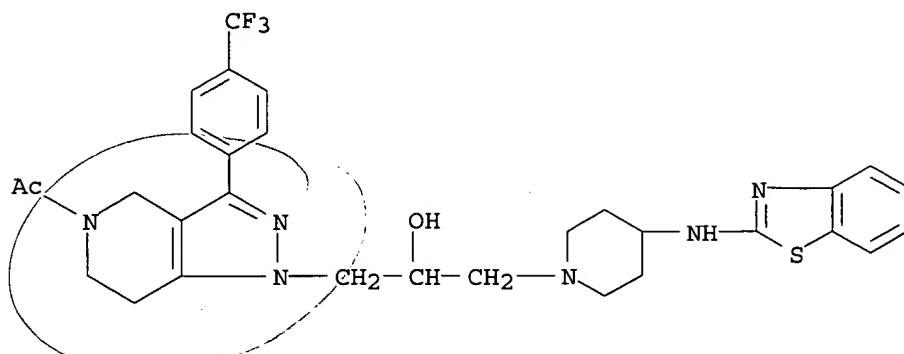
IT **400797-30-0P**, 1-[1-[3-[4-(Benzothiazol-2-ylamino)piperidin-1-yl]-2-hydroxypropyl]-3-(4-trifluoromethylphenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone **400797-65-1P**, 1-[1-[3-[5-Methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]propyl]piperidin-4-yl]-3,4-dihydro-1H-quinazolin-2-one  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antiallergy agent; prepn. of phenylpyrazolopyridines as cathepsin S inhibitors for treating allergies)

RN 400797-30-0 CAPLUS

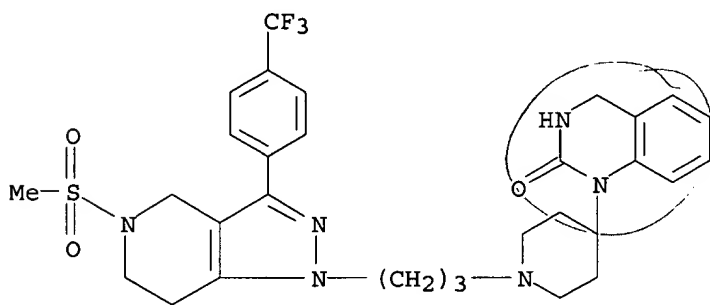
CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-.alpha.-[[4-(2-benzothiazolylamino)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

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RN 400797-65-1 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine, 1-[3-[4-(3,4-dihydro-2-oxo-1(2H)-quinazolinyl)-1-piperidiny]propyl]-4,5,6,7-tetrahydro-5-(methylsulfonyl)-3-[4-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)



L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:142709 CAPLUS

DOCUMENT NUMBER: 136:200183

TITLE: Substituted and/or fused pyrazoles, particularly indolylpiperidinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants

INVENTOR(S): Cai, Hui; Edwards, James P.; Meduna, Steven P.; Pio, Barbara A.; Wei, Jianmei

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014317	A2	20020221	WO 2001-US25180	20010810
WO 2002014317	A3	20020704		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

applicants

09/288,556

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
AU 2001084823 A5 20020225 AU 2001-84823 20010810  
US 2002040019 A1 20020404 US 2001-927188 20010810  
EP 1309592 A2 20030514 EP 2001-963912 20010810  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
PRIORITY APPLN. INFO.: US 2000-225178P P 20000814  
US 2001-927188 A ~~20010810~~  
WO 2001-US25180 W 20010810  
OTHER SOURCE(S): MARPAT 136:200183  
GI

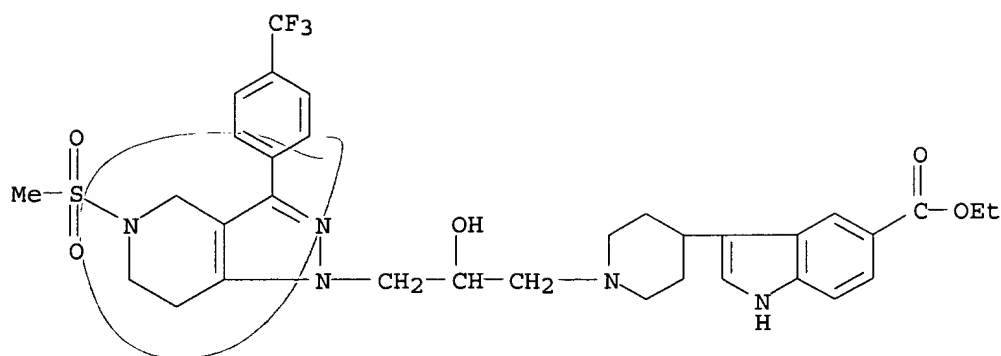
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Substituted pyrazoles I, methods of manufg. them, compns. contg. them, and methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [W, X, Y, Z = N, (un)substituted CH (0-3 of them may be N; or 1 can be N-oxide when other 3 .noteq. N); R = H, alkyl, cyano, hydroxyalkyl, acyl, CHO, alkoxy carbonyl, or (un)substituted carbamoyl; R1, R2 = H, alkyl; R3, R4 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R3R4 = atoms to form (un)substituted (un)satd. (non)arom. 5- to 7-membered carbo- or heterocyclic ring; Ar = (un)substituted mono- or bicyclic (hetero)aryl; n = 0-2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); Q = O, S, (un)substituted NH; including stereoisomers, pharmaceutically acceptable salts, esters, and amides]. Claimed uses include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 70 individual compds. I were prepd. and/or claimed, with detailed prepn. given for 13 compds. For instance, 6-(morpholin-4-yl)-3-(piperidin-4-yl)-1H-pyrrolo[3,2-c]pyridine (prepd. in 5 steps) reacted with the corresponding epoxide (prepd. in several steps) to give title compd. II, a preferred compd. In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.02 .mu.M. Compd. III is another one of four specifically preferred compds.

IT **400801-53-8P**, 3-[1-[2-Hydroxy-3-[5-methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]propyl]piperidin-4-yl]-1H-indole-5-carboxylic acid ethyl ester  
**400801-58-3P**, 1-[5-Methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-3-[4-(5-oxy-1H-pyrrolo[3,2-c]pyridin-3-yl)piperidin-1-yl]propan-2-ol  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug candidate; prepn. of indolylpiperidinylpropyl-substituted pyrazolopyridines and analogs as cathepsin S inhibitors)

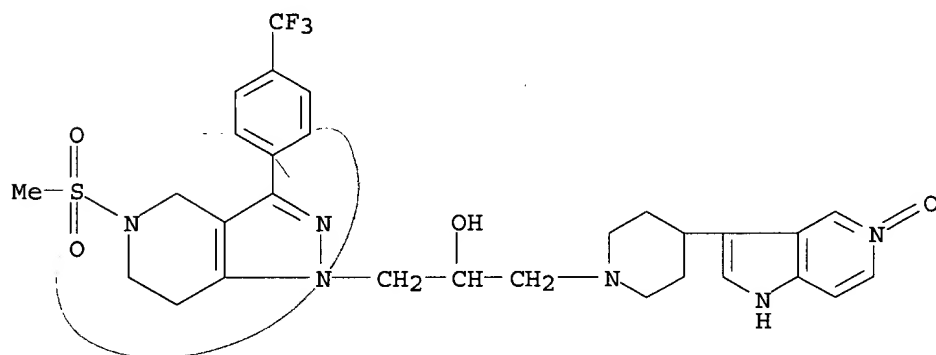
RN **400801-53-8** CAPLUS  
CN 1H-Indole-5-carboxylic acid, 3-[1-[2-hydroxy-3-[4,5,6,7-tetrahydro-5-(methylsulfonyl)-3-[4-(trifluoromethyl)phenyl]-1H-pyrazolo[4,3-c]pyridin-1-yl]propyl]-4-piperidinyl]-, ethyl ester (9CI) (CA INDEX NAME)





RN 400801-58-3 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 4,5,6,7-tetrahydro-5-(methylsulfonyl)-.alpha.-[[4-(5-oxido-1H-pyrrolo[3,2-c]pyridin-3-yl)-1-piperidinyl]methyl]-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:142708 CAPLUS

DOCUMENT NUMBER: 136:200182

TITLE: Substituted and/or fused pyrazoles, particularly piperidinypropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants

INVENTOR(S): Butler, Christopher R.; Cai, Hui; Edwards, James P.; Grice, Cheryl A.; Gustin, Darin J.; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sehon, Clark A.; Tays, Kevin L.; Wei, Jianmei

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 235 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014315	A2	20020221	WO 2001-US25290	20010810
WO 2002014315	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,  
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,  
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001086454 A5 20020225 AU 2001-86454 20010810  
 US 2003078419 A1 20030424 US 2001-927324 20010810  
 EP 1309593 A2 20030514 EP 2001-965898 20010810

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
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PRIORITY APPLN. INFO.:

US 2000-225178P-P-20000814  
 US 2001-927324 A 20010810  
 WO 2001-US25290 W 20010810

OTHER SOURCE(S): MARPAT 136:200182

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Substituted pyrazoles I, methods of manufg. them, compns. contg. them, and methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [R = H, OH, or absent; R1, R2 = H, alkyl; R3, R4 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R3R4 = atoms to form (un)substituted (un)satd. (non)arom. 5- to 7-membered carbo- or heterocyclic ring; Ar1 = (un)substituted mono- or bicyclic (hetero)aryl; Ar2 = (un)substituted (un)satd. (non)arom. mono- or bicyclic ring system with 0-5 heteroat. ring moieties selected from O, S, N, SO2, and CO; n = 0-2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); W = O, S, CO CONH, NHCO, (un)substituted NH or CH2; including stereoisomers, pharmaceutically acceptable salts, esters, and amides]. Claimed usages include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 350 individual compds. I were prepd. and/or claimed, with detailed prepn. given for 31 compds. For instance, 6-chloro-1-(piperidin-4-yl)-3,4-dihydro-1H-quinolin-2-one (prepd. in 6 steps) reacted with the corresponding epoxide (prepd. in several steps) to give title compd. II. In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.01 .mu.M. Compd. III is one of two specifically preferred compds.

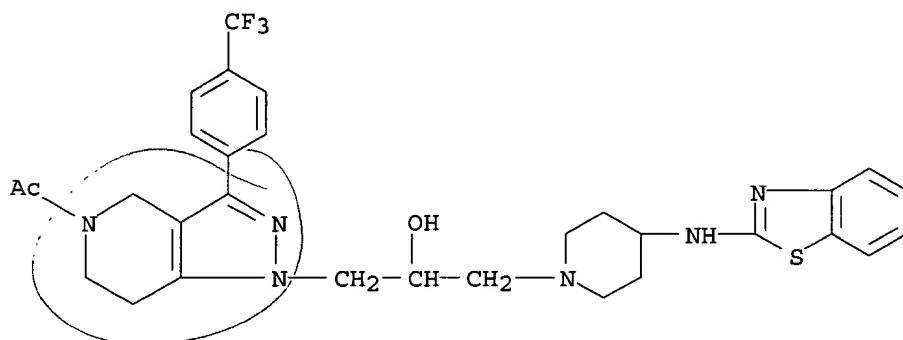
IT **400797-30-0P**, 1-[1-[3-[4-(Benzothiazol-2-ylamino)piperidin-1-yl]-2-hydroxypropyl]-3-(4-trifluoromethylphenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone **400797-65-1P**, 1-[1-[3-[5-Methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]propyl]piperidin-4-yl]-3,4-dihydro-1H-quinazolin-2-one **400798-30-3P**, 1-[1-[3-[5-Acetyl-3-(4-bromophenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yl]-6-chloro-3,4-dihydro-1H-quinolin-2-one **400798-35-8P**, 1-[1-[3-[4-(6-Chloro-2,2-dioxo-2,3-dihydro-2.lambda.6-2,1,3-benzothiadiazol-1-yl)piperidin-1-yl]-2-hydroxypropyl]-3-(4-trifluoromethylphenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone **400798-44-9P**, 4-[1-[3-[3-(4-Bromophenyl)-5-methanesulfonyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yl]-6-chloro-4H-1,4-benzoxazin-3-one **400798-59-6P**, 1-[1-[3-[5-Acetyl-3-(4-nitrophenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yl]-1,3-dihydroindol-2-one **400798-73-4P**, 1-[3-(4-Chloro-3-methylphenyl)-1-[2-hydroxy-3-[4-(2-methyl-2,3-dihydroindol-1-yl)piperidin-1-yl]propyl]-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone

**400799-11-3P**, N-[1-[3-[5-Acetyl-3-(4-chloro-3-methylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yl]-N-(3-chlorophenyl)acetamide **400799-21-5P**, 1-[3-(4-Chlorophenyl)-1-[2-hydroxy-3-[4-(3-methoxyphenylamino)piperidin-1-yl]propyl]-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone **400799-26-0P**, [2-[[1-[3-[3-(4-Bromophenyl)-5-(methanesulfonyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]propyl]piperidin-4-yl]amino]-4-(ethanesulfonyl)phenoxy]acetic acid methyl ester **400799-42-0P**, 2-[1-[3-(4-Bromophenyl)-5-methanesulfonyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yloxy]benzonitrile **400799-49-7P**, 1-[1-[3-[5-Acetyl-3-(4-iodophenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yl]-1,3-dihydrobenzimidazol-2-one **400799-57-7P**, 1-[1-[3-[5-Acetyl-3-(4-chloro-3-methylphenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]piperidin-4-yl]-3-ethyl-1,3-dihydrobenzimidazol-2-one **400799-65-7P**, 1-[2-Hydroxy-3-[4-(2-oxo-2,3-dihydrobenzimidazol-1-yl)piperidin-1-yl]propyl]-3-(4-trifluoromethylphenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridine-5-carboxylic acid amide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; prepn. of piperidinylpropyl-substituted pyrazolopyridines and analogs as cathepsin S inhibitors)

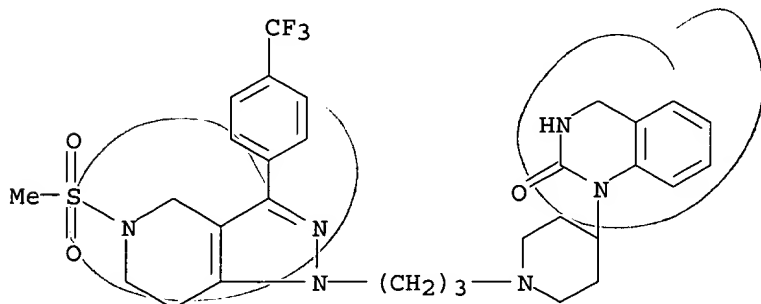
RN 400797-30-0 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine, 1-[3-[4-(3,4-dihydro-2-oxo-1(2H)-quinazolinyl)-1-piperidinyl]propyl]-4,5,6,7-tetrahydro-5-(methylsulfonyl)-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 400797-65-1 CAPLUS

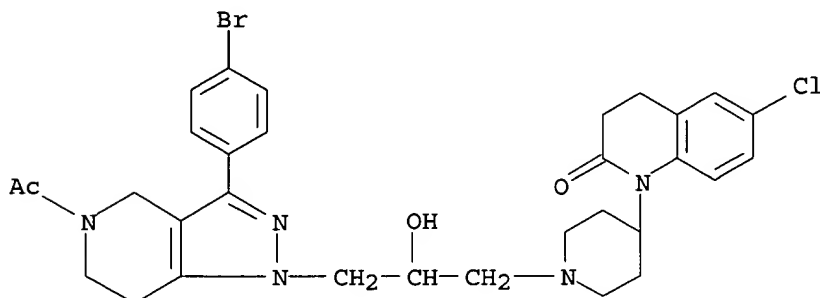
CN 1H-Pyrazolo[4,3-c]pyridine, 1-[3-[4-(3,4-dihydro-2-oxo-1(2H)-quinazolinyl)-1-piperidinyl]propyl]-4,5,6,7-tetrahydro-5-(methylsulfonyl)-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



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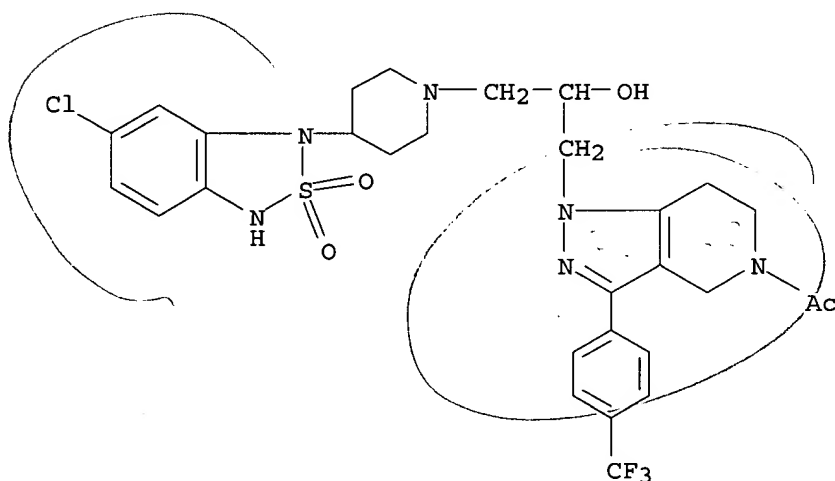
RN 400798-30-3 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-3-(4-bromophenyl)-.alpha.-[[4-(6-chloro-3,4-dihydro-2-oxo-1(2H)-quinolinyl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



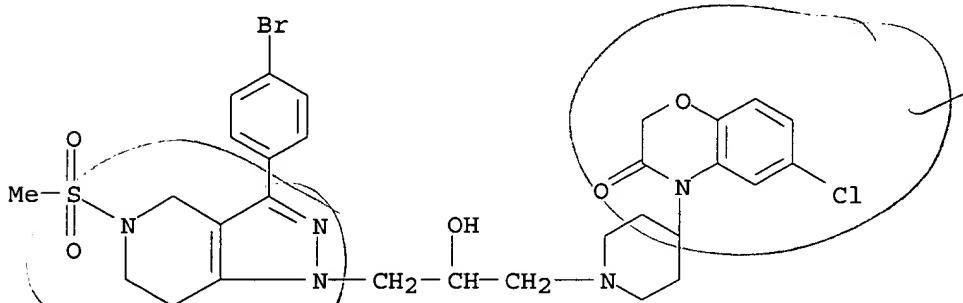
RN 400798-35-8 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-.alpha.-[[4-(6-chloro-2,2-dioxido-2,1,3-benzothiadiazol-1(3H)-yl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 400798-44-9 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 3-(4-bromophenyl)-.alpha.-[[4-(6-chloro-2,3-dihydro-3-oxo-4H-1,4-benzoxazin-4-yl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro-5-(methylsulfonyl)- (9CI) (CA INDEX NAME)

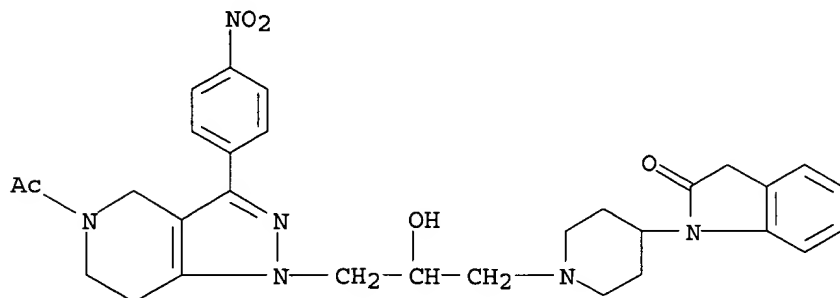


RN 400798-59-6 CAPLUS

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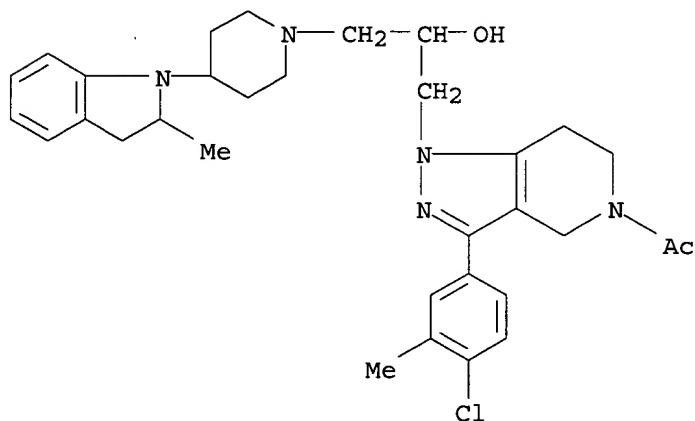
09/288,556

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-.alpha.-[[4-(2,3-dihydro-2-oxo-1H-indol-1-yl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro-3-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



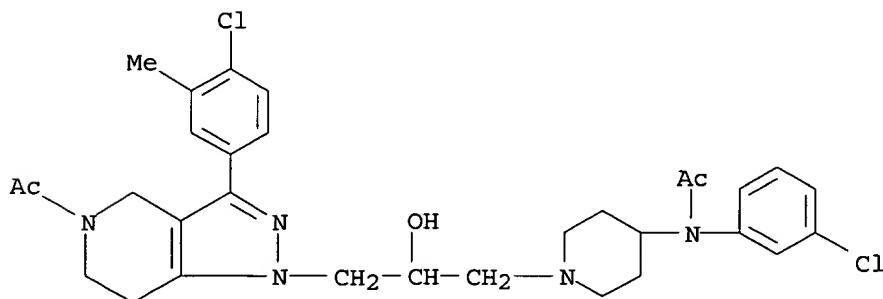
RN 400798-73-4 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-3-(4-chloro-3-methylphenyl)-.alpha.-[[4-(2,3-dihydro-2-methyl-1H-indol-1-yl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



RN 400799-11-3 CAPLUS

CN Acetamide, N-[1-[3-[5-acetyl-3-(4-chloro-3-methylphenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridin-1-yl]-2-hydroxypropyl]-4-piperidinyl]-N-(3-chlorophenyl)- (9CI) (CA INDEX NAME)

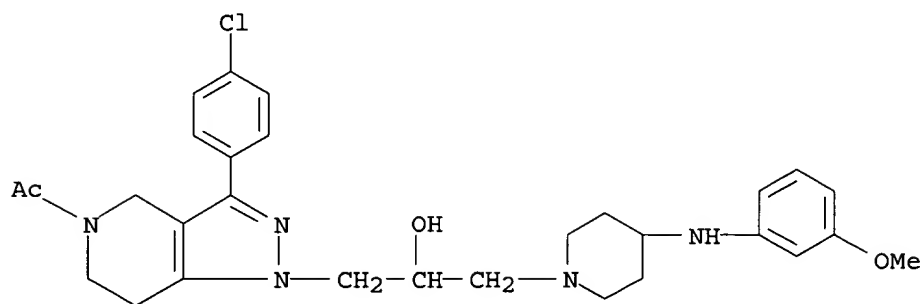


RN 400799-21-5 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-3-(4-chlorophenyl)-4,5,6,7-

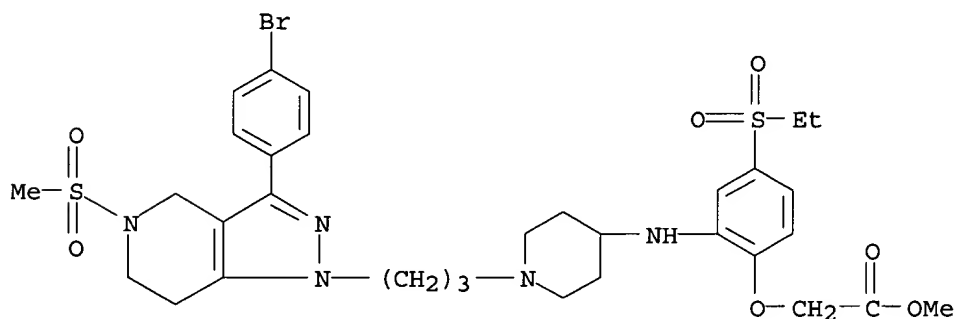
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tetrahydro-.alpha.-[[4-[(3-methoxyphenyl)amino]-1-piperidinyl]methyl]-  
(9CI) (CA INDEX NAME)



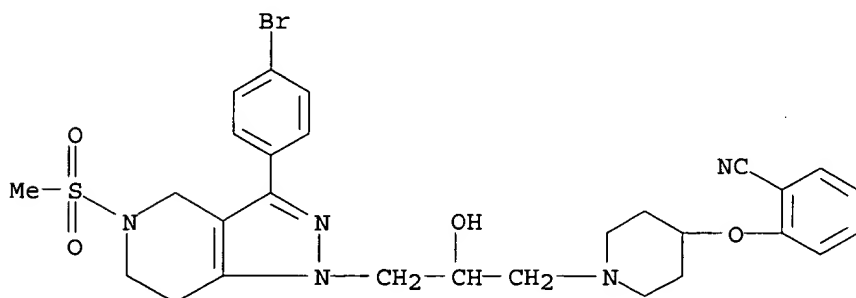
RN 400799-26-0 CAPLUS

CN Acetic acid, [2-[[1-[3-[3-(4-bromophenyl)-4,5,6,7-tetrahydro-5-(methylsulfonyl)-1H-pyrazolo[4,3-c]pyridin-1-yl]propyl]-4-piperidinyl]amino]-4-(ethylsulfonyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 400799-42-0 CAPLUS

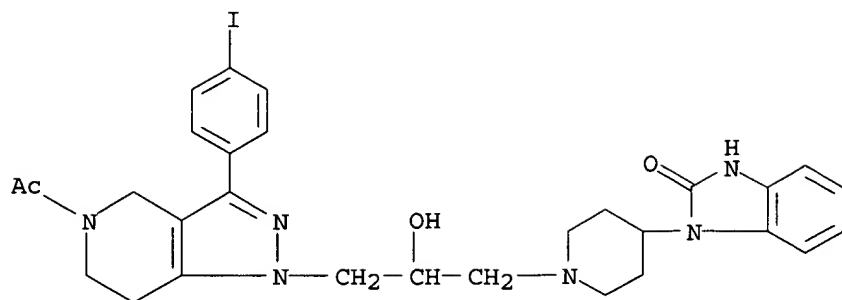
CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 3-(4-bromophenyl)-.alpha.-[[4-(2-cyanophenoxy)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro-5-(methylsulfonyl)-  
(9CI) (CA INDEX NAME)



RN 400799-49-7 CAPLUS

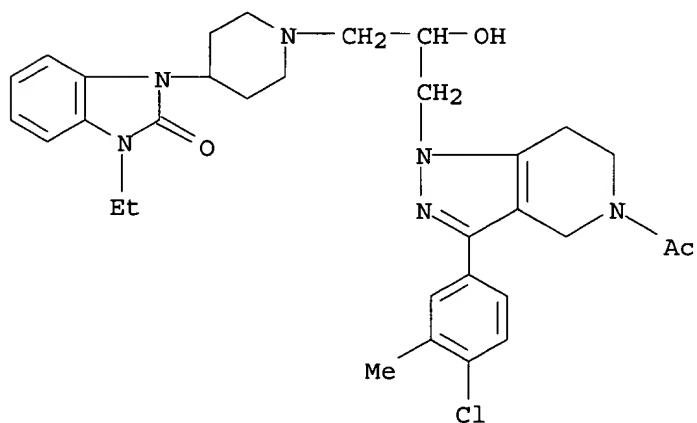
CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-.alpha.-[[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro-3-(4-iodophenyl)-  
(9CI) (CA INDEX NAME)

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RN 400799-57-7 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-3-(4-chloro-3-methylphenyl)-.alpha.-[[4-(3-ethyl-2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)



RN 400799-65-7 CAPLUS

CN 5H-Pyrazolo[4,3-c]pyridine-5-carboxamide, 1-[3-[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]-2-hydroxypropyl]-1,4,6,7-tetrahydro-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

